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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/240,455	01/29/99	MUNDSCHENK	D 15050.5

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HM22/1107

EXAMINER

WARE, T

ART UNIT	PAPER NUMBER
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1615

DATE MAILED:

11/07/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.

09/240,455

Applicant(s)

MUNDSCHEK, DAVID D.

Examiner

Todd D Ware

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

## Status

- 1) ☒ Responsive to communication(s) filed on 06 October 2000.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-69 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 and 3-69 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some \* c) ☐ None of the CERTIFIED copies of the priority documents have been:
1. ☐ received.
2. ☐ received in Application No. (Series Code / Serial Number) \_\_\_\_\_.
3. ☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5,7.
- 18) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

Art Unit: 1615

### **DETAILED ACTION**

Receipt of information disclosure statement filed 10-6-00 and request for extension of time (granted), information disclosure statement, and amendment all filed 8-11-00 is acknowledged. Claims 1, 3, and 7-9 have been amended as requested. Claim 2 has been canceled and new claims 11-69 have been added. Claims 1 and 3-69 are pending.

### ***Claim Objections***

Claims 37, 43, 57, 63 are objected to because of the following informalities: each of these claims depends from plural claims (i.e. claim 37 depends from claims 7. It appears that these are typographical errors as each claim appears to be intended to only depend from one claim and not plural claims. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-4, 9-50, 52-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mundshenk et al (WO 97/43407; hereafter '407 in combination with Heiber et al (US 5,766,620; hereafter '620) and further in combination with Cardinaux et al (US 5,578,567; hereafter '567).

'407 teaches a method of preparing inactivated toxins and bioactive peptides and methods for their administration involving inactivation of a toxin or bioactive peptide with

Art Unit: 1615

ozone and administering the inactivated peptide parenterally as a vaccination. These peptides may be prepared by the use of ozonated water to prevent the formation of disulfide bridges. The method of '407 also uses the method of preparing a cDNA strand encoding the peptide. For toxins, see the table in column 5. For protein hormones, see the paragraph bridging columns 4 and 5. '407 does not teach buccal administration of the peptides or inclusion of a quaternary ammonium salt such as benzalkonium chloride for enhancing mucosal absorption of the peptide in the buccal cavity.

'620 is relied upon for teaching that peptides are buccally administratable. '620 employs adhesive tablets containing a peptide and a permeation enhancer to deliver the peptides buccally.

'567 is relied upon for teaching mucosal peptide formulations that contain benzalkonium chloride as a preservative.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '407, '620, and '567 to provide a non-invasive route of administration for inactivated peptides to vaccinate an individual that contains benzalkonium chloride to protect the composition against bacterial contamination. Manipulation of the amount of benzalkonium chloride to include in the formulation would be obvious to one skilled in the art in an effort to maximize the antibacterial properties of benzalkonium chloride.

Claims 1, 3-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mundshenk et al (WO 97/43407; hereafter '407 in combination with Kamiya et al (US

Art Unit: 1615

4,948,588; hereafter '588) and further in combination with Cardinaux et al (US 5,578,567; hereafter '567).

'407 is relied upon for all that it teaches as previously stated. '407 does not teach buccal administration of the peptides or inclusion of a quaternary ammonium salt such as benzalkonium chloride for enhancing mucosal absorption of the peptide in the buccal cavity.

'588 is relied upon for teaching buccal administration of peptides by spraying compositions of peptides with absorption enhancing agents in aerosol and non-aerosol formulations.

'567 is relied upon for teaching mucosal peptide formulations that contain benzalkonium chloride as a preservative.

Accordingly, it would have been obvious to one skilled in the art at the time of the invention to combine the teachings of '407, '588, and '567 to provide a non-invasive route of administration for inactivated peptides to vaccinate an individual that contains benzalkonium chloride to protect the composition against bacterial contamination. Manipulation of the amount of benzalkonium chloride to include in the formulation would be obvious to one skilled in the art in an effort to maximize the antibacterial properties of benzalkonium chloride.

### ***Response to Arguments***

Art Unit: 1615

Applicant's arguments filed 8-11-00 have been fully considered but they are not persuasive. Applicant argues that the references are unrelated and fail to teach a combination to arrive at the methods and formulations of the instant claims.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

It is submitted that indeed the references are related. Mundshenk et al ('407) teaches peptide formulations, while Heiber et al ('620), Kamiya et al ('588), and Cardinaux et al ('567) teach methods of administering peptide formulations and a means of preserving the formulations. Inclusion of benzalkonium chloride in such a combined formulation would inherently provide the enhanced mucosal absorption of the peptide in the buccal cavity. Indeed, benzalkonium chloride is known to assist in the absorption of medicinal agents through the mucosa and into the blood stream (Acharya, US 5,686,094; column 9, lines 25-29). Such a statement is further supported by the experiments of Costa et al (1997) and Fang et al (1998) who demonstrate that benzalkonium chloride is effective at enhancing the transdermal permeation of lorazepam and enoxacin, respectively. Dondeti et al (1995) demonstrates that spray

Art Unit: 1615


formulations containing benzalkonium chloride provide for higher absorption of insulin when compared to the same formulation without benzalkonium chloride. Furthermore, Siegel et al (1985) demonstrates that surfactants such as benzalkonium chloride increase the penetration rate of compounds across oral mucosa. Accordingly, the rejection is maintained.

### **Conclusion**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Todd D Ware whose telephone number is (703) 305-1700. The examiner can normally be reached on 8:30-5:00

  
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